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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,481	AHMAD ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 6-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3/27/03.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper filed June 02, 2003 is acknowledged. Claims 3-5 and 14-26 have been cancelled as requested in amendment of paper submitted June 02, 2003.

The traversal is on the ground(s) that the search of the art relevant to the inventions of Groups III-VI would be directly related to art of Group I. This is not found persuasive for those reasons of record in section 2 of Paper No. 11. Specifically, in accordance with 37 C.F.R. § 1.475 (d), the ISA/US considers that any feature which is the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and, therefore, each of such products and methods defines a separate invention. Furthermore, because during the further examination claim 1, as written, encompasses subject matter known in prior art, it cannot serve as a unifying technical feature and, consequently, Group I would have been properly restricted to the proteins only.

Also, the traversal of the restriction requirement is moot in view of the cancellation of the claims directed to the non-elected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-2 and 6-13 are pending in the instant application.

Claims 1-2 and 6-13 are under examination in the instant office action.

Specification

2. The text of the instant specification is objected because: on page 6, line 21 "R1C3 receptor protein" should be "B1C3 receptor protein, perhaps. Clarification is required.

Claim Objections

3. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 10 depends from claim 9, which is limited to a host cell transformed with a nucleic acid encoding a protein of SEQ ID NO: 1, while claim 10 encompasses a B1C3 receptor. Therefore, claim 10 can be infringed by a protein, which does not infringe claim 9. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the nucleic acid claims could be infringed without infringing the claims from which it depends, i.e. the protein claims. Therefore, they are improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-2 and 6-13 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is

> insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an isolated nucleic acid molecule and the protein encoded thereby of as yet undetermined function or biological significance. It is clear from the instant specification that the claimed novel nucleic acid encodes "a novel G protein-coupled receptor that is structurally distinct from previously reported receptors. It is referred to herein as the "B1C3 receptor" (page 1, last paragraph of the instant specification). More specifically, B1C3 receptor (SEQ ID NO: 1) is about 34% homologous to mouse EDG-1 receptor and about 33% homologous to the rat EDG-1 receptor (see description of Figure 3 on page 3). Therefore, based on the structural similarities to different known proteins from GPCR family of receptors, it has been suggested that the B1C3 receptor of the instant invention would also possess similar biological activity. Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

In the absence of knowledge of the biological significance of this specific nucleic acid and encoded protein, there is no immediately obvious patentable use for the polynucleotide or the encoded protein. According to the specification of the instant application "[o]ne of the main uses for B1C3 nucleic acids and recombinant proteins is in assays designed to identify agents capable of binding to the receptor", and further, "[t]hese agents have potential therapeutic application as either analgesics or anesthetics" (page 9, third paragraph of the instant specification). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant nucleic acid or encoded protein is associated with any pain-related function or pathology. To employ the DNA and the protein in the future methods generation of antibodies or "to screen for drug candidates using cell signaling assays" is not a "real world" utility because it would eventually relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the protein as a marker for any specific disease or condition (which would be a real world use). Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the modulation of the biological effects of B1C3 receptor by alteration of "the extent to which the receptor is expressed in cells" (last paragraph on page 12), would have any clinical practical application. To employ a nucleic acid and the protein encoded thereby of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein in their currently available form, then the

claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 and 6-13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, because claims 1 and 6 encompass proteins and polynucleotides with "additions, deletions or substitutions which do not substantially alter the functional characteristics of the receptor" (see the definition of "consisting essentially of" on page 1, last paragraph of the instant specification), the instant specification is also not enabling because one can not following the guidance presented therein and practice the claimed invention without first making the substantial inventive contribution at determining which amino acids in SEQ ID NO: 1 are critical to the functional and structural integrity of B1C3 receptor and which amino acids are expendable.

6. Claims 1-2 and 6-13 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to proteins comprising the amino acid sequence consisting functionally of SEQ ID NO: 1. Claim 6 is directed to polynucleotides encoding proteins comprising the amino acid sequence consisting functionally of SEQ ID NO: 1. Claims 2 and 7-13 are dependent claims. According to the instant specification "[t]he term "consisting essentially of" refers to proteins in which the sequence of SEQ ID NO: 1 has undergone additions, deletions or substitutions which do not substantially alter the functional characteristics of the receptor" (last paragraph on page 1). However, the instant specification fails to describe the entire genus of proteins and polynucleotides, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 1. This nucleic acid molecule has a nucleic acid sequence of SEQ ID NO: 2. The subject matter, which is claimed is described above. The claims are drawn to proteins and nucleic acids with additions, deletions or substitutions which do not substantially alter the functional characteristics of the receptor. First, the claims are not limited to a protein with a specific amino acid sequence. The claims only require proteins and polynucleotides to share some degree of structural similarity to the protein of SEQ ID NO: 1 and polynucleotide of SEQ IDNO: 2. The specification only describes a protein having the amino acid sequence of

SEQ ID NO: 1 and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO: 1 and has the "the functional characteristics of the receptor".

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the protein of SEQ ID NO: 1 and polynucleotide of SEQ ID NO: 2. The specification does not provide a complete structure of those polypeptides and polynucleotides with "additions, deletions or substitutions which do not substantially alter the functional characteristics of the receptor". The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus (those proteins with "additions, deletions or substitutions which do not substantially alter the functional characteristics of the receptor") because the specification teaches only the one embodiment of SEQ ID NO: 1. Therefore, the claims are directed to subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-2 and 6-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1 and 6 are vague and ambiguous for using "comprising" and "consisting" language within one claim. The metes and bounds of the claimed subject matter cannot be defined from the claims or the instant specification.

9. Claim 10 recites the limitation " B1C3 receptor " in claim 9. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 10 is further vague and indefinite in so far as it employs the term "B1C3 receptor" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "B1C3 receptor". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "B1C3 receptor", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

11. Claims 2, 7-9 and 11-13 are indefinite for being dependent from indefinite claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Nenonene et al., 1994 (J. Neurochem., Vol..62, No. 5, pp.1822-1834).

Claim 1 is directed to a protein, except as existing in nature, comprising the amino acid sequence of SEQ ID NO: 1. The term "except as existing in nature", according to the instant specification refers to a protein in a purified state (see page 2, first paragraph). Nenonene et al. disclose rat brain membrane preparations, see page 1823, second column, last paragraph, for example. Because the instant claimed protein is a naturally occurring protein, which is expressed in rat central nervous system (see page 7, second and third paragraphs of the instant specification), the membrane preparations of Nenonene et al. clearly represent this protein in a purified state. Thus, Nenonene et al. anticipated claim 1 of the instant application.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-7939. Official papers should NOT be faxed to (703) 308-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.